201-15413

Anh Nguyen
06/28/2004 01:53 PM

To: NCIC HPV@EPA
cc:
Subject: Fw: Revised Robust Summary and Test Plan for Fluorobenzene, CAS#462-06-6

----- Forwarded by Anh Nguyen/DC/USEPA/US on 06/28/2004 01:52 PM -----

Edwin L Mongan <Edwin.L.Mongan-1@USA.dupont.com>
06/25/2004 03:42 PM

To: NCIC OPPT@EPA, Rtk Chem@EPA, Jim_Keith@americanchemistry.com
cc: Mike Kaplan <Mike.Kaplan@USA.dupont.com>
Subject: Revised Robust Summary and Test Plan for Fluorobenzene, CAS#462-06-6

Dear Sir or Madam:

We are submitting the attached cover letter and revised version of the HPV Robust Summary and Test Plan for the compound fluorobenzene, in response to comments received from EPA. Please replace the HPV documents currently posted on EPA's web site with these revised versions. If you have any questions, please let me know.

With Best Regards,

Edwin L. Mongan
Manager, Environmental Stewardship
(See attached file: Fluorobenzene Resubmission.pdf)

Fluorobenzene Resubmission.pdf

201-15413

Safety, Health & Environment Excellence Center
1007 Market Street, DuPont 6082
Wilmington, DE 19898
302-773-0910 (Office) – 302-774-3140 (Fax)
Edwin.L.Mongan-1@usa.dupont.com

May 5, 2004

Marianne Lamont Horinko, Administrator
U.S. Environmental Protection Agency
P.O. Box 1473
Merrifield, VA 2216

Attn: Chemical Right-to-Know Program

Re: EPA comments on the Test Plan and Robust Data Summary Fluorobenzene

Dear Administrator Horinko,

E. I. du Pont de Nemours & Company, Inc. received EPA's comments on the test plan and robust data summary Fluorobenzene, CAS# 462-06-6, and is pleased to respond. We have considered the recommended revisions to environmental fate, health effects and ecological effects, and we revised our submittal as needed on the attached summary sheet. Also included with this submittal is a revised robust data summary.

Please feel free to contact me with any questions or concerns you may have with regards to this submission at Edwin.L.Mongan-1@usa.dupont.com or by phone at 302-773-0910.

Sincerely,

Edwin L. Mongan, III
Manager, Environmental Stewardship
DuPont Safety, Health & Environment

Cc: Charles Auer – U.S. EPA
Office of Pollution Prevention & Toxics
U. S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

(May 4, 2004)

Fluorobenzene: Response to EPA Comments

General

EPA comment: For both health and ecological effects, the submitter needs to provide a justification for the analogs used. For health, the submitter needs to provide justification using robust summaries for the comparison of metabolism data, repeated-dose studies, and physicochemical characteristics of the two chemicals (fluorobenzene and chlorobenzene).

Response: Physicochemical characteristics, repeated dose studies, reproduction study and metabolism of chlorobenzene were added to the document.

Environmental Fate

EPA comment: *Stability in water.* EPA assumes that the submitter will provide the proposed hydrolysis data following OECD TG 111.

Response: The proposed hydrolysis test will follow OECD TG 111.

EPA comment: *Biodegradation.* Estimated data are not adequate for the purposes of the HPV Challenge Program. The submitter needs to provide measured ready biodegradation data following OECD TG 301.

Response: Urano and Kato (1986), using a 14-day MITI format BOD test equivalent to OECD TG 301 C, demonstrated that no fluorobenzene biodegradation occurred. In addition, Carvalho et al (2002) report that microbial mineralization of fluorobenzene will occur in less than four months, based on enrichments from sediments near industrial outfalls in northern Portugal. The use of a standardized format by Urano and Kato (1986) is sufficient to satisfy the need for ready biodegradation data following OECD TG 301. The observed failure of fluorobenzene to degrade in the 14-day test and the observations of Carvalho et al (2002) means that fluorobenzene has the potential to be inherently biodegradable, but is not readily biodegradable. This is in general agreement with modeling estimates. No additional biodegradation testing is proposed for fluorobenzene.

Health Effects

EPA comment: *Closed system intermediate status.* The submitter needs to provide additional information to satisfy the requirements for classification of fluorobenzene as a 'closed system intermediate.' If the claim cannot be supported, then EPA recommends a combined repeated-dose/reproductive/developmental toxicity screening test (OECD 421).

Response: While DuPont handles fluorobenzene as a closed system intermediate, DuPont cannot guarantee that all fluorobenzene users maintain the same level of controls. This robust summary contains the developmental and reproductive toxicity data for the

structurally related compound, chlorobenzene to meet the developmental and reproductive toxicity endpoints.

EPA comment: *Acute Toxicity*. Information from Eitington and Ulanova, 1975 should not be used in the test plan and robust summaries since the studies are considered unreliable.

Response: Reference was moved to the additional references section of the document.

EPA comment: *Repeated-Dose Toxicity*. A robust summary for a 28-day inhalation assay in rats lacked details and did not include the specific hematological, clinical chemistry and urinalysis parameters assessed, and the identity of the organs weighed and evaluated for histopathology.

Response: Additional details were added to the robust summary.

EPA comment: *Genetic Toxicity - Mutations*. The submitter should delete the sentence that states that fluorobenzene is not mutagenic in the Ames assay. Both studies are adequate and the issue of a positive response with hamster S9 in one study is not invalidated by the other study which relied on rat S9 only.

Response: The summary was revised to indicate that the response was equivacol.

EPA comment: *Genetic Toxicity – Chromosome aberrations*. A robust summary for a negative micronucleus assay in mice did not provide sufficient information to evaluate the study. The study is mischaracterized as 'medium' when 'not assignable' is more appropriate. The secondary source should be located and summarized or the additional information which was not utilized should be included.

Response: Additional details were added to the robust summary and the reliability was reassessed based on the new information.

EPA comment: *Developmental Toxicity*. A robust summary for a developmental study in rats exposed by inhalation to the analog chlorobenzene needs to include information on the magnitude of the reduction in body weight gain in high-concentration dams and GLP status.

Response: The magnitude of the reduction in body weight gain in the high concentration dams was added to the robust summary. GLP status was indicated as unknown in the robust summary because the published paper did not state if the study was conducted according to GLP.

Ecological Effects

EPA comment: *Acute Toxicity to Fish.* The studies submitted on fluorobenzene and chlorobenzene are inadequate. The studies were not performed in a closed system or with suitable monitoring of test substance and the chemical's loss during the test was not accounted for in both tests.

Response: The acute test with goldfish utilized a static renewal design with test solution renewals every 12 hours. The vapor pressure of fluorobenzene is approximately 60 mm Hg at approximately 20°C. Although the test concentrations were not measured, the test solution renewal frequency in the goldfish study was sufficient to provide an accurate assessment of aquatic toxicity.

EPA comment: *Invertebrates*. Missing study details for the studies of fluorobenzene and analogs (1-chloro-2-fluorobenzene, 1-chloro-3-fluorobenzene, and 1-chloro-4-fluorobenzene) in *Daphnia magna* included the test system (i.e. static or renewal), test concentrations, number of daphnia per concentration (fluorobenzene), loading, endpoint that was evaluated (e.g. immobility), number of deaths and/or proportion of animals that displayed the signs of toxicity per concentration, an the test conditions (e.g. temperature and dissolved oxygen).

Response: Additional data were added to the robust summaries if it was available in the published papers.

EPA comment: *Algae*. EPA reserves judgment on the adequacy of submitted algae study on chlorobenzene (analog) pending submission of missing critical data elements. For the validity of the test, the cell concentration in the control cultures should have increased by the factor of at least 16 within three days. Missing study details noted in the summary for the study of chlorobenzene in *Selenastrum capricornutum* included test substance purity, number of replicates per concentration, use and response of control cultures, statistical methods, lighting, pH, and cell concentrations per test concentration at each measurement interval, and 95% confidence limits.

Response: The authors of the cited study reported that the test medium and test conditions were similar to those prescribed in US EPA, 1971 except that the temperature was maintained at 20±1°C.